

## Supplementary Information

### **Genome-wide SNP and CNV analysis identifies common and low-frequency variants associated with severe early-onset obesity**

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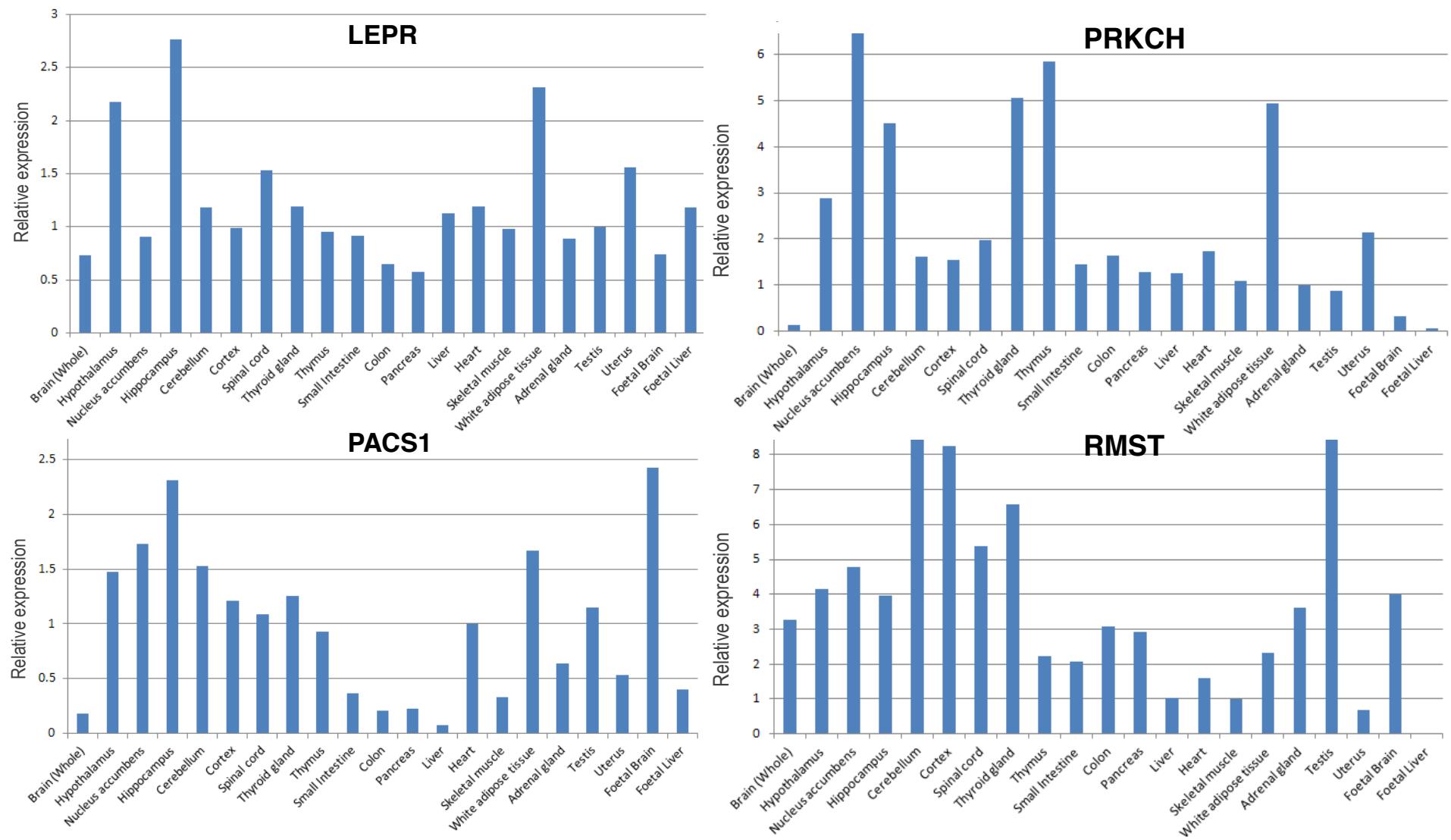
**Supplementary Table 6.** Pathway enrichment analysis of rare genic obesity CNVs.

**Supplementary Table 7.** Pathway enrichment analysis of rare genic obesity CNVs. Geneset enrichment p-values for each of the enriched pathway categories are shown (*p*-value <0.05).

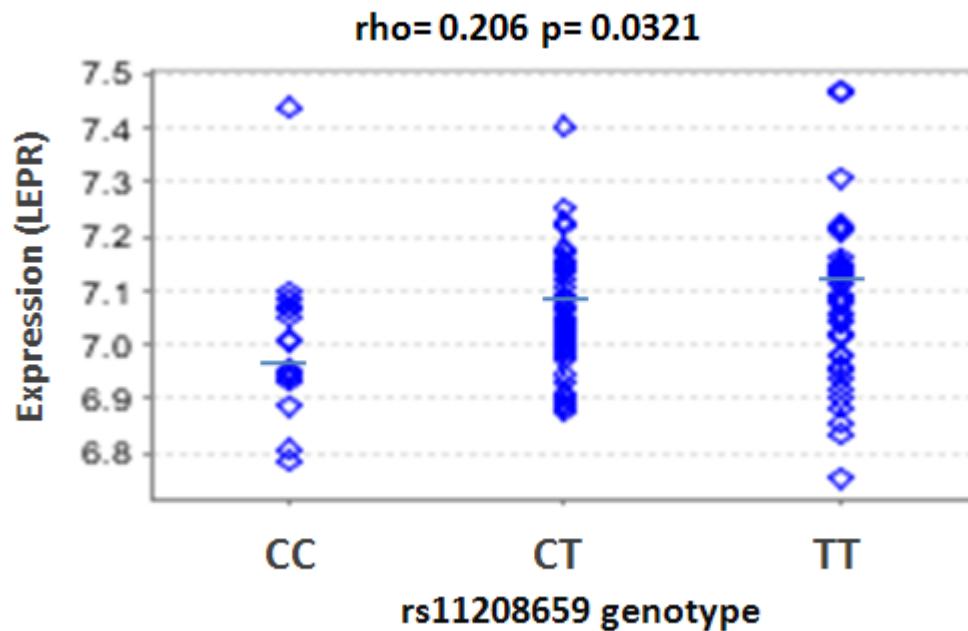
**Supplementary Table 8.** Oligonucleotides used for the EMSA experiment.

## Supplementary References

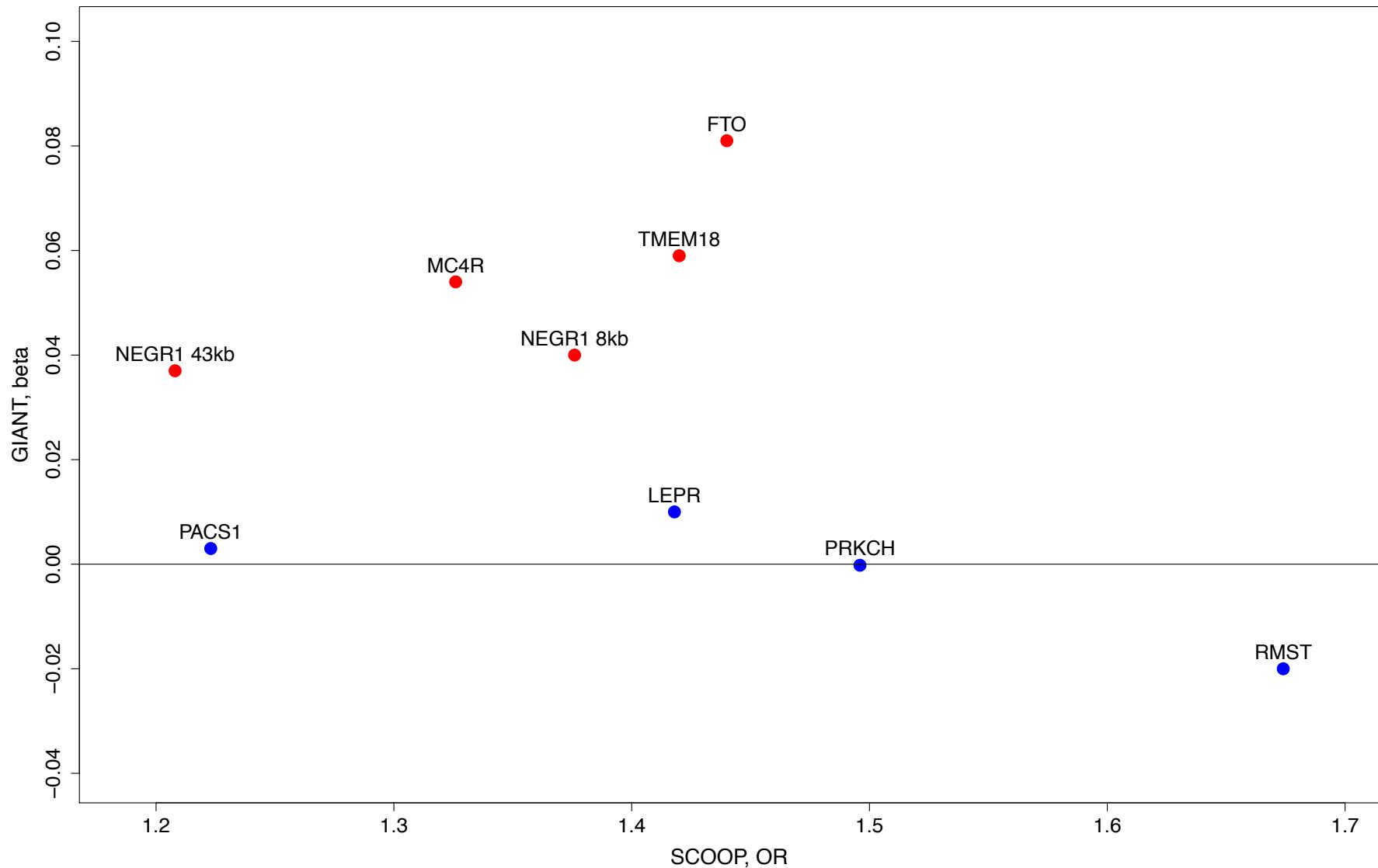
**Supplementary Figure 1.** Expression pattern of the genes in the newly identified obesity-associated GWAS loci across human tissues. The expression was measured using the DeltaDeltaCt method, normalized to a housekeeping gene (beta-actin) and the relative expression to median is shown.



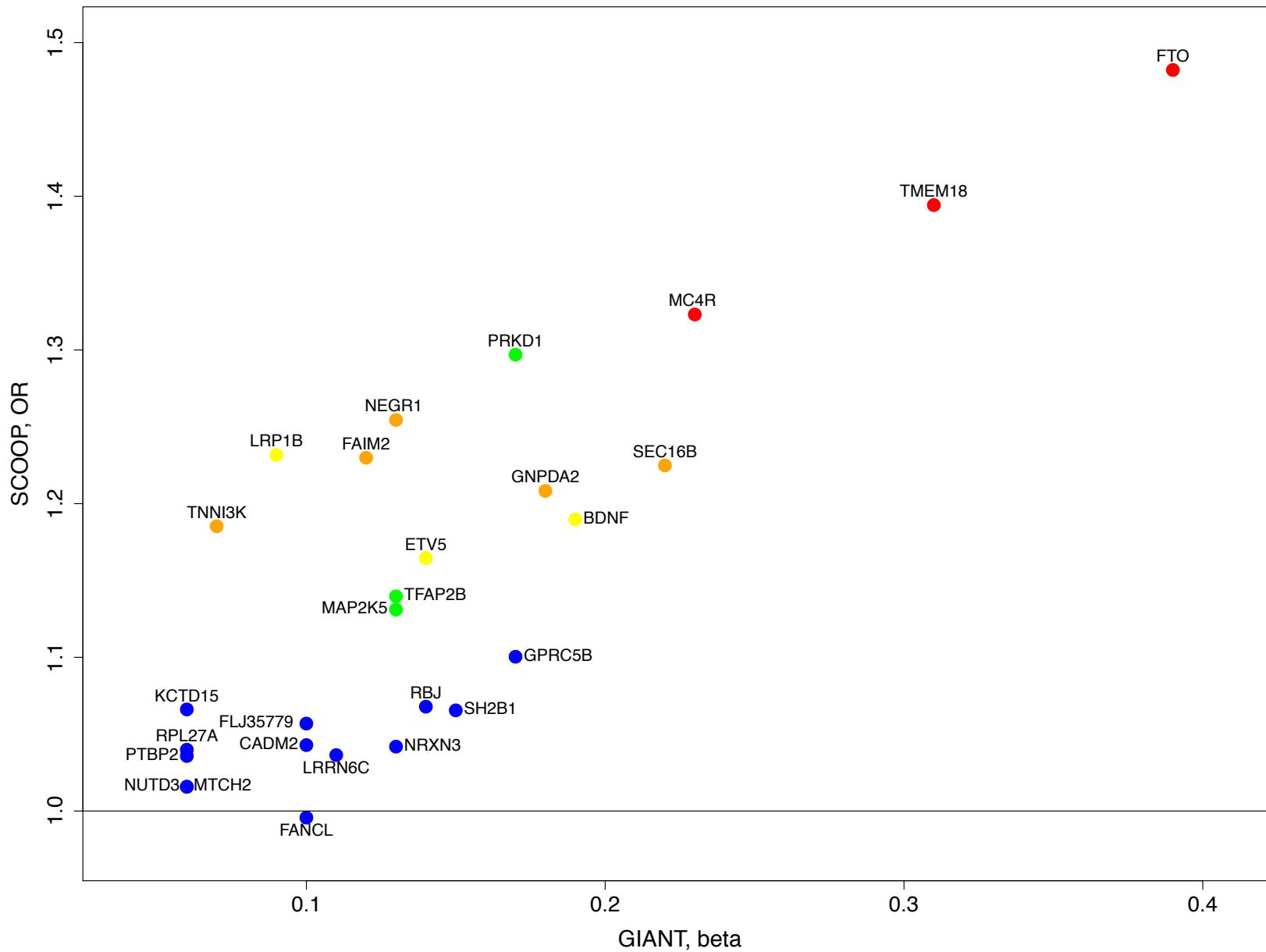
**Supplementary Figure 2.** Expression quantitative trait loci (eQTL) at the LEPR locus of chromosome 1p31.1. GENEVAR software plots are shown for the lead SNP correlating with LEPR expression (rs11208659). The risk allele 'C' is associated with lower LEPR expression. Statistical values are shown in accordance with GENEVAR calculations for correlation between SNP genotype and LEPR expression, median values are noted (S1). Expression of LEPR mRNA in lymphoblastoid cell lines from the 108 HapMap Yoruba subjects (YRI) is plotted. rho – Spearman's rank correlation coefficient, Student t-test p-values.



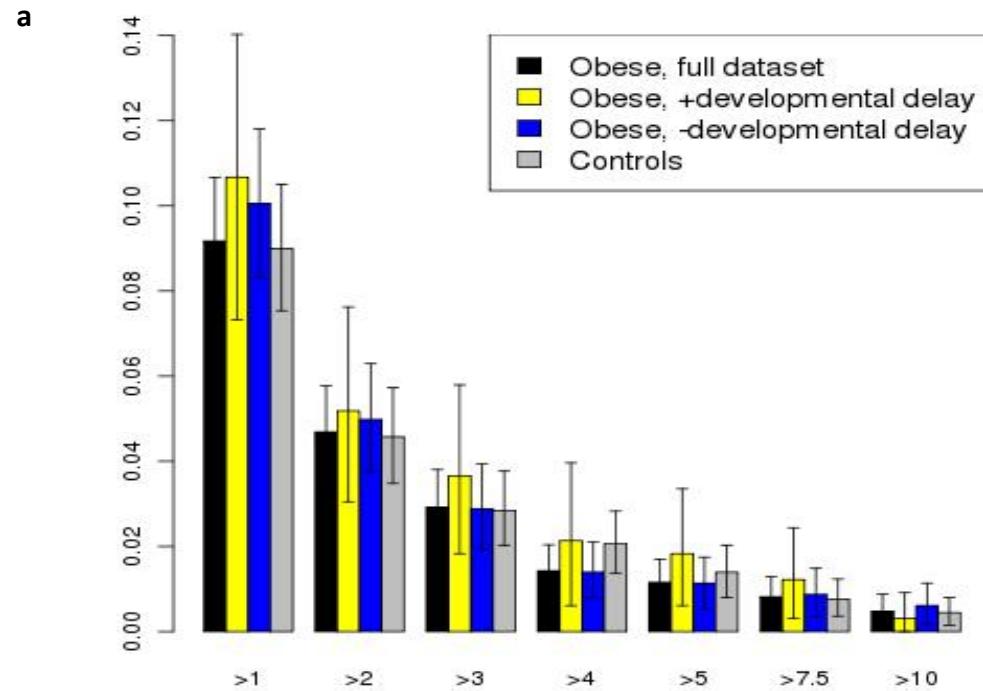
**Supplementary Figure 3.** Odds ratios in SCOOP vs. per-allele beta-coefficients for BMI in GIANT. Points are coloured according to the significance of the SNP in the GIANT BMI results:  $p < 5 \times 10^{-8}$  (red),  $5 \times 10^{-8} \leq p < 1 \times 10^{-4}$  (orange),  $1 \times 10^{-4} \leq p < 0.01$  (yellow),  $0.01 \leq p < 0.05$  (green) and  $0.05 \leq p < 1$  (blue).



**Supplementary Figure 4.** Per-allele beta-coefficients for BMI in GIANT vs. odds ratios in SCOOP. Points are coloured according to the significance of the SNP in the SCOOP results:  $p < 5 \times 10^{-8}$  (red),  $5 \times 10^{-8} \leq p < 1 \times 10^{-4}$  (orange),  $1 \times 10^{-4} \leq p < 0.01$  (yellow),  $0.01 \leq p < 0.05$  (green) and  $0.05 \leq p < 1$  (blue).



**Supplementary Figure 5. a.** Proportion of individuals with one or more region of HBD greater than set size thresholds (1-10MB). Error bars represent 95% confidence intervals. **b.** P.values derived from Fisher's Exact Test using the same data.

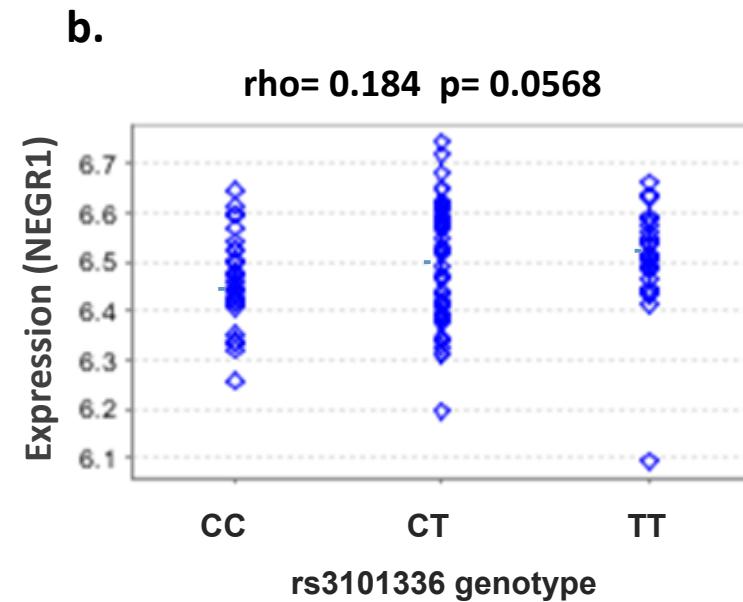
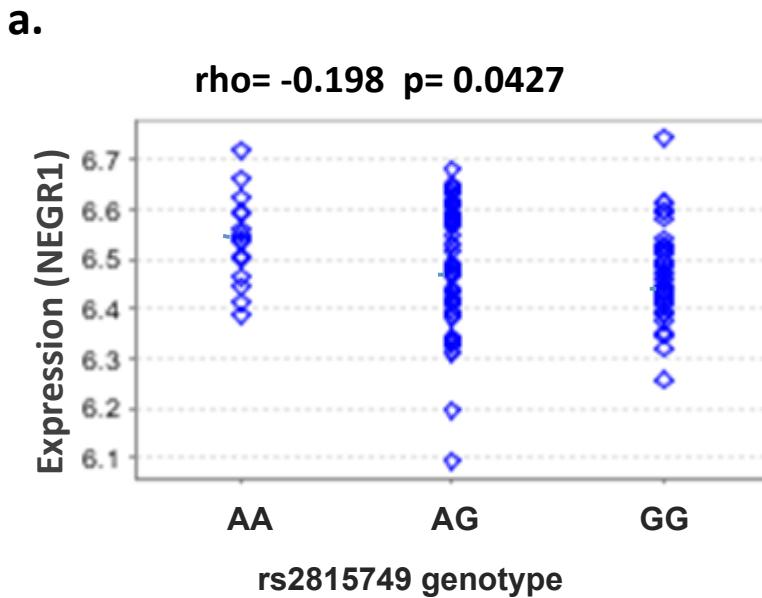


**b**

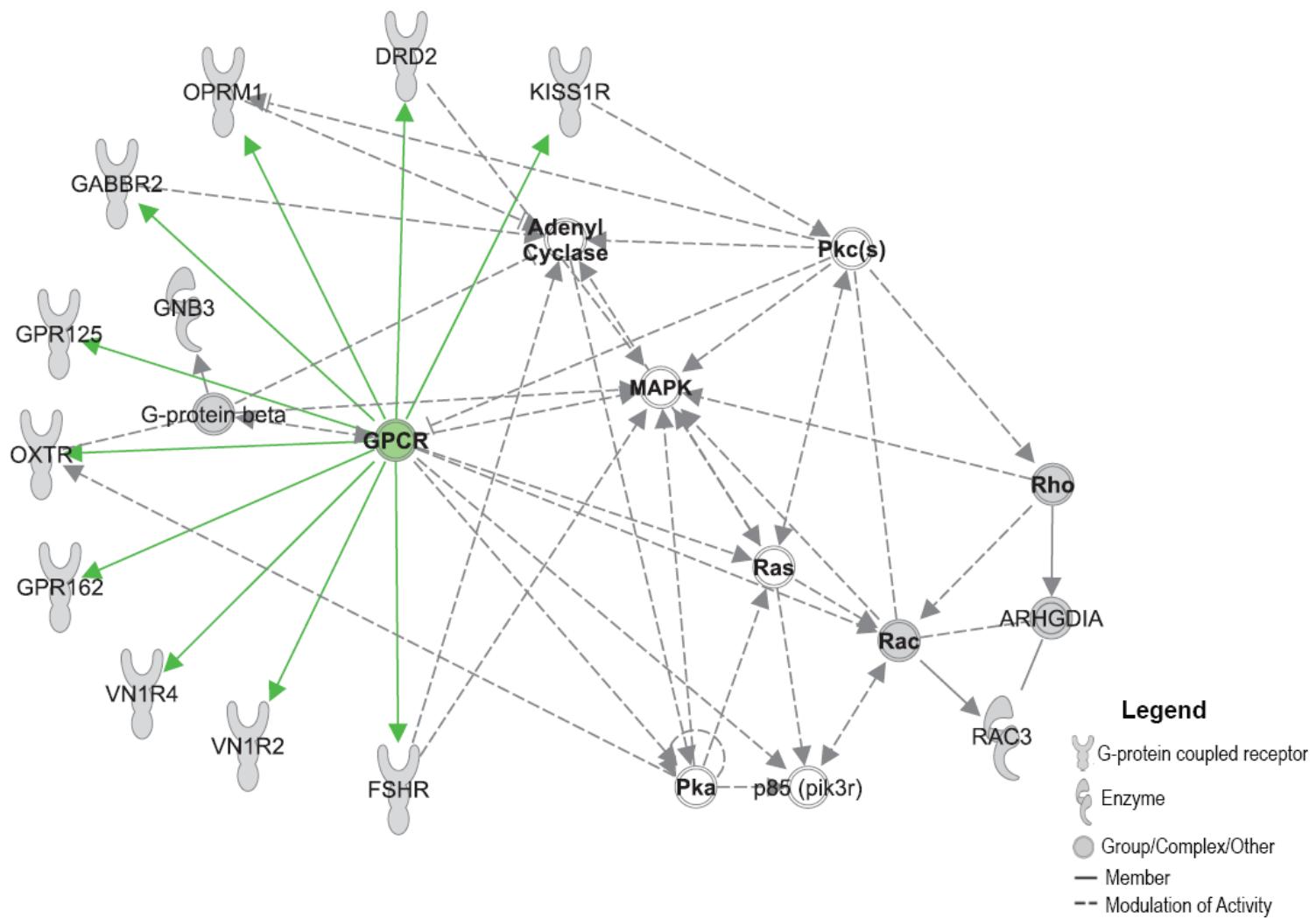
	Size Threshold	Control/Obese+DD	Control/Obese-DD	Obese+DD/Obese-DD
	>1MB	0.15	0.09	0.68
	>2MB	0.4	0.3	0.89
	>3MB	0.29	0.69	0.47
	>4MB	0.68	0.28	0.32
	>5MB	0.45	0.77	0.4
	>7.5MB	0.3	0.57	0.52
	>10MB	1	0.34	1

**Supplementary Figure 6. Expression quantitative trait loci (eQTL) at the NEGR1 locus on 1p31.1.** GENEVAR association plots are shown for the correlation between SNPs tagging the two deletions and NEGR1 expression in lymphoblastoid cell lines in 108 YRI HapMap subjects (S2).

**a.** rs2815749 tags the small 8-kb deletion (allele A). **b.** rs3101336 tags the large 43-kb deletion (allele C). Median values noted; p - Student t-test nominal p-value.

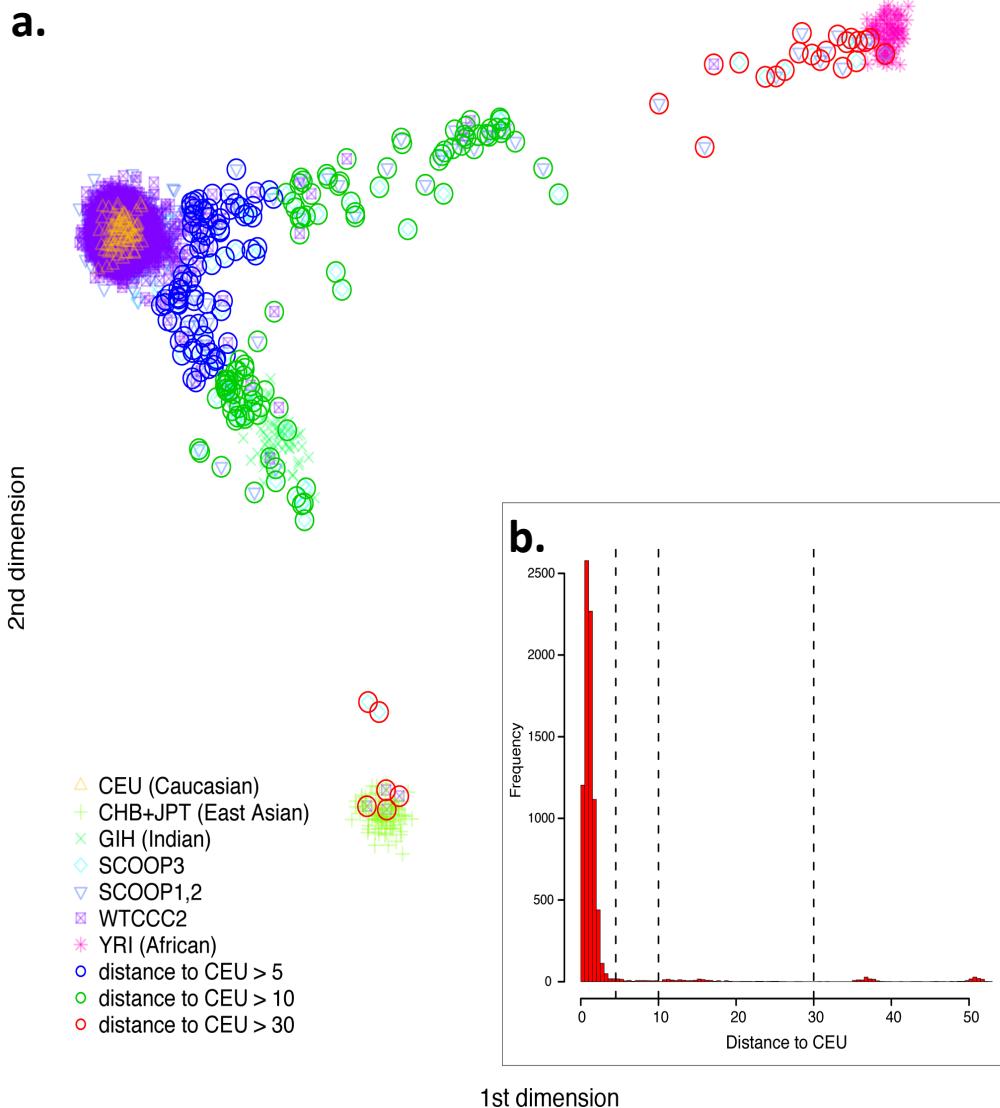


**Supplementary Figure 7.** Rare CNV pathway analysis using Ingenuity Pathway analysis software. The most statistically significant obesity-associated category involves genes encoding several G-protein coupled receptors (green), shown in the context of the respective downstream signalling pathways. Specific genes deleted in SCOOP are highlighted in grey.



## Supplementary Figure 8. Identifying ethnic outliers based on SNP genotypes and MDS projection.

**a.** Each small symbol represents a sample. The European, East Asian and African populations are well separated and serve as reference points for samples of unknown ethnicity. As a positive control, the Indian population is located approximately at the midpoint of the European-East Asian axis, which is consistent with its ethnic and geographical relationship with the two reference populations. All cases and controls, including those failed sample QC or removed by various filters, are displayed. Red, green and blue circles highlight samples regarded as non-European under thresholds of different stringency, shown as dashed lines in **b.** the distribution of the distance between the European reference population and all samples (including the reference populations).



Supplementary Table 1. Discovery, follow-up & combined results for the 29 SNPs taken forward for validation. Of those 27 SNPs met the  $p<1\times10^{-6}$  threshold, with the other 2 SNPs having good genotypecluster & regional plots warranting further investigation. <sup>a</sup>Positions according to Build 36. <sup>b</sup>Replication HWE p-value in cases =  $3.9\times10^{-7}$ . <sup>c</sup>Replication MAF controls = 0.008

SNP	Nearest gene	Chr.	Position (bp) <sup>a</sup>	Discovery						Replication						Discovery + Replication					
				IMPUTED	Effect allele	Other allele	P-value		EAF controls	Proxy used	P-value		EAF controls	SNP	Effect	StdErr	P-value		Direction		
							(discovery)	(EAFCases)			(replication)	(EAFCases)					(discovery + replication)	(EAFCases)			
rs1421085	FTO	16	52358455	0	C	T	1.49 (1.37 - 1.61)	8.38E-22	0.50	0.41	1.36 (1.22 - 1.51)	<b>4.656E-08</b>	0.48	0.40	rs1421085	0.3645	0.0331	1.44 (1.35 - 1.54)	<b>3.072E-28</b>	--	
rs476828	MC4R	18	56003567	0	C	T	1.33 (1.21 - 1.46)	1.91E-09	0.29	0.24	1.32 (1.16 - 1.50)	<b>1.637E-05</b>	0.27	0.22	rs476828	0.2822	0.0379	1.33 (1.23 - 1.43)	<b>9.381E-14</b>	--	
rs12463617	TMEM18	2	619244	1	C	A	1.43 (1.27 - 1.60)	7.70E-10	0.89	0.85	1.40 (1.19 - 1.65)	<b>4.799E-05</b>	0.87	0.83	rs12463617	0.3504	0.0475	1.42 (1.29 - 1.56)	<b>1.697E-13</b>	--	
rs1993709	NEGR1 ( <i>tagging 10kb CNV</i> )	1	72611117	1	G	A	1.46 (1.32 - 1.63)	1.98E-12	0.87	0.81	1.22 (1.05 - 1.41)	<b>0.0107</b>	0.85	0.82	rs1993709	0.3193	0.0442	1.38 (1.26 - 1.5)	<b>5.086E-13</b>	--	
rs1957894	PRKCH	14	60977864	0	T	G	1.64 (1.39 - 1.95)	1.01E-08	0.08	0.06	1.34 (1.11 - 1.61)	<b>0.0022</b>	0.10	0.08	rs1957894	0.403	0.0642	1.5 (1.32 - 1.7)	<b>3.349E-10</b>	++	
rs11208659	LEPR	1	65751868	1	C	T	1.63 (1.40 - 1.88)	1.16E-10	0.11	0.08	1.15 (0.96 - 1.38)	<b>0.1175</b>	0.10	0.09	rs11208659	0.3495	0.0581	1.42 (1.27 - 1.59)	<b>1.838E-09</b>	--	
rs564343	PACS1	11	65651742	0	A	G	1.25 (1.16 - 1.36)	5.81E-08	0.47	0.41	1.17 (1.05 - 1.30)	<b>0.0057</b>	0.44	0.40	rs564343	0.2014	0.0336	1.22 (1.15 - 1.31)	<b>2.032E-09</b>	++	
rs11109072	RMST	12	96425401	1	A	C	1.79 (1.44 - 2.22)	1.48E-07	0.05	0.03	1.50 (1.13 - 1.99)	<b>0.0044</b>	0.04	0.03	rs11109072	0.0152	0.0877	1.67 (1.41 - 1.99)	<b>4.211E-09</b>	++	
rs3101336	NEGR1 ( <i>tagging 40kb CNV</i> )	1	72523773	1	C	T	1.26 (1.16 - 1.37)	5.28E-08	0.66	0.60	1.12 (1.00 - 1.25)	<b>0.0472</b>	0.64	0.61	rs3101336	0.1892	0.0338	1.21 (1.13 - 1.29)	<b>2.206E-08</b>	--	
rs1048466	CCDC77	12	421811	0	G	A	1.30 (1.18 - 1.42)	3.46E-08	0.77	0.72	1.11 (0.98 - 1.25)	<b>0.1120</b>	0.74	0.72	rs1048466	0.2021	0.0377	1.22 (1.14 - 1.32)	<b>8.048E-08</b>	--	
rs16923476	OTUD1/KIAA1217	10	23898217	1	A	G	2.08 (1.60 - 2.70)	3.69E-08	0.04	0.02	1.31 (0.91 - 1.89)	<b>0.1474</b>	0.02	0.02	rs16923476	0.5775	0.1084	1.78 (1.44 - 2.2)	<b>9.928E-08</b>	++	
rs17025867	SLC8A1 <sup>b</sup>	2	40432063	1	A	G	2.41 (1.81 - 3.20)	1.40E-09	0.03	0.02	1.14 (0.79 - 1.64)	<b>0.4842</b>	0.02	0.02	rs17025867	0.5959	0.1144	1.81 (1.45 - 2.27)	<b>1.882E-07</b>	++	
rs3782724	SCNN1A	12	6336342	0	G	A	1.60 (1.33 - 1.93)	8.49E-07	0.07	0.04	1.28 (1.00 - 1.63)	<b>0.0473</b>	0.06	0.04	rs3782724	0.3865	0.0754	1.47 (1.27 - 1.71)	<b>2.968E-07</b>	--	
rs9328321	FARS2	6	5545437	0	A	G	1.26 (1.14 - 1.38)	5.05E-06	0.25	0.21	rs9504450	1.16 (1.02 - 1.32)	<b>0.0211</b>	0.25	0.22	rs9328321	0.1997	0.0399	1.22 (1.13 - 1.32)	<b>5.457E-07</b>	++
rs2275848	NINJ1	9	94927141	0	T	G	1.39 (1.25 - 1.55)	2.67E-09	0.86	0.82	1.01 (0.88 - 1.16)	<b>0.8638</b>	0.81	0.81	rs2275848	0.2101	0.0435	1.23 (1.13 - 1.34)	<b>0.000001349</b>	++	
rs1631486	TCF4	18	51177355	1	A	G	1.31 (1.20 - 1.42)	7.48E-10	0.38	0.31	0.98 (0.87 - 1.1)	<b>0.7118</b>	0.36	0.37	rs1631486	0.1618	0.0351	1.18 (1.1 - 1.26)	<b>0.000003919</b>	+	
rs187365	FOXF1	16	85069416	0	C	T	1.34 (1.21 - 1.49)	5.87E-08	0.86	0.82	1.01 (0.87 - 1.17)	<b>0.8648</b>	0.83	0.83	rs187365	0.1981	0.0438	1.22 (1.12 - 1.33)	<b>0.000006195</b>	--	
rs12408810	PRMT6	1	106442466	0	C	T	1.48 (1.30 - 1.67)	1.12E-09	0.91	0.87	0.96 (0.82 - 1.12)	<b>0.5857</b>	0.86	0.87	rs12408810	0.2232	0.0502	1.25 (1.13 - 1.38)	<b>0.000008806</b>	+	
rs190392	CHN2	7	29316532	1	T	C	1.73 (1.48 - 2.03)	5.36E-12	0.10	0.07	0.75 (0.60 - 0.93)	<b>0.0101</b>	0.06	0.08	rs190392	0.2692	0.0653	1.31 (1.15 - 1.49)	<b>0.000003737</b>	+	
rs4766856	KSR2	12	116459662	0	T	C	1.26 (1.15 - 1.37)	1.21E-07	0.40	0.34	0.99 (0.88 - 1.11)	<b>0.7989</b>	0.37	0.38	rs4766856	0.143	0.0348	1.15 (1.08 - 1.24)	<b>0.000003847</b>	+	
rs10012946	WFS1	4	6344251	0	C	T	1.22 (1.12 - 1.32)	3.96E-06	0.64	0.60	1.04 (0.93 - 1.17)	<b>0.4774</b>	0.60	0.59	rs10012946	0.1417	0.0345	1.15 (1.08 - 1.23)	<b>0.000004109</b>	--	
rs10271846	AMPH	7	38611029	1	G	A	1.31 (1.18 - 1.45)	4.45E-07	0.21	0.18	0.98 (0.85 - 1.13)	<b>0.8056</b>	0.18	0.18	rs10271846	0.1699	0.0429	1.19 (1.09 - 1.29)	<b>0.000007424</b>	+	
rs4315494	ID2	2	8363828	1	A	G	1.41 (1.24 - 1.61)	3.61E-07	0.92	0.89	rs11887635	0.98 (0.83 - 1.16)	<b>0.8270</b>	0.89	0.89	rs4315494	0.2063	0.0536	1.23 (1.11 - 1.37)	<b>0.0001175</b>	+
rs4936406	DSCAML1	11	117123647	0	T	C	1.73 (1.41 - 2.11)	1.21E-07	0.98	0.95	0.95 (0.74 - 1.21)	<b>0.6676</b>	0.95	0.95	rs4936406	0.3057	0.0797	1.36 (1.16 - 1.59)	<b>0.0001266</b>	--	
rs9819360	OSBPL10	3	31729342	0	C	A	1.23 (1.13 - 1.33)	8.89E-07	0.45	0.40	0.99 (0.89 - 1.10)	<b>0.8254</b>	0.40	0.41	rs9819360	0.1269	0.0336	1.14 (1.06 - 1.21)	<b>0.0001592</b>	+	
rs17017873	CRIM1	2	36020348	1	C	G	1.96 (1.54 - 2.48)	2.62E-08	0.04	0.02	0.90 (0.69 - 1.18)	<b>0.4555</b>	0.04	0.05	rs17017873	0.3379	0.0913	1.4 (1.17 - 1.68)	<b>0.0002136</b>	+	
rs17201502	FAIM2	12	48571829	0	T	C	1.24 (1.14 - 1.35)	3.77E-07	0.40	0.35	0.97 (0.86 - 1.08)	<b>0.5529</b>	0.36	0.37	rs17201502	0.126	0.0343	1.13 (1.06 - 1.21)	<b>0.000243</b>	+	
rs2117842	HS1BP3/RHOB	2	20624550	0	C	G	1.37 (1.22 - 1.55)	2.02E-07	0.90	0.87	rs6714202	0.90 (0.77 - 1.06)	<b>0.2046</b>	0.86	0.87	rs2117842	0.1664	0.0489	1.18 (1.07 - 1.3)	<b>0.0006753</b>	+
rs7255638	ZNF586 <sup>c</sup>	19	62981821	0	T	C	1.82 (1.47 - 2.25)	2.77E-08	0.98	0.96	0.33 (0.21 - 0.52)	<b>1.113E-06</b>	0.97	0.97	rs7255638	0.282	0.0974	1.33 (1.1 - 1.6)	<b>0.00381</b>	+	

Supplementary Table 2. Results for SNPs previously found to be associated with varying degrees of obesity.

\*Results for the G/C SNP rs6235 are reported on the opposite strand in SCOOP. †GPR120 region was imputed using the Jun 2011, 1000 genomes EUR reference panel, rs116454156 failed imputation QC.

‡ This gene was originally identified through an analysis of BMI in the population. A subset of the discovery SCOOP samples contributed to the evidence that MC4R was associated with extreme obesity.

Published obesity loci						SCOOP Discovery						
SNP	Gene	Phenotype	Reference	Effect allele	Other allele	SNP	Effect allele	Other allele	OR (95% CI)	P-value	EAF cases	EAF controls
rs1421085	<i>FTO</i>	severe obesity	Frayling et al. Science Dina et al. Nat Genet 2007	C	T	rs1421085	C	T	1.49 (1.37 - 1.61)	8.38E-22	0.5039814	0.4054708
rs17782313	<i>MC4R</i> <sup>¶</sup>	extreme obesity	Loos et al., Nat Genet 2008	C	T	rs17782313	C	T	1.32 (1.21 - 1.45)	4.99E-09	0.286994	0.2346483
rs6232 (N221D)	<i>PCSK1</i>	extreme obesity	Benzinou et al., Nat Genet 2008	C	T	No proxy SNP						
rs6235 (S690T)	<i>PCSK1</i>	extreme obesity	Benzinou et al., Nat Genet 2008	C	G	rs6235	G*	C	1.08 (0.99 - 1.19)	0.0810166	0.2945206	0.2787925
rs1805081	<i>NPC1</i>	extreme obesity	Meyre et al., Nat Genet 2009	G	A	rs1805081	C	T	0.96 (0.89 - 1.05)	0.372873	0.4121668	0.4200917
rs1424233	<i>MAF</i>	extreme obesity	Meyre et al., Nat Genet 2009	A	G	rs1424233	T	C	1.06 (0.97 - 1.15)	0.180004	0.4773484	0.4636924
rs10508503	<i>PTER</i>	extreme obesity	Meyre et al., Nat Genet 2009	C	T	rs10508503	C	T	1.01 (0.87 - 1.16)	0.926391	0.9141816	0.9139245
rs4712652	<i>PRL</i>	extreme adult obesity	Meyre et al., Nat Genet 2009	A	G	No proxy SNP						
rs6548238	<i>TMEM18</i>	childhood obesity	Scherag et al. PLOS Genetics 2010	C	T	rs6548238	C	T	1.40 (1.25 - 1.56)	2.63E-09	0.8748327	0.8298631
rs12145833	<i>SDCCAG8</i>	childhood extreme obesity	Scherag et al. PLOS Genet 2010	T	G	rs12145833	T	G	1.04 (0.93 - 1.17)	0.450353	0.8585156	0.8526786
rs17150703	<i>TNKS/MSRA</i>	childhood extreme obesity	Scherag et al. PLOS Genet 2010	A	G	rs17150703	A	G	1.08 (0.95 - 1.24)	0.2487	0.1093439	0.1023234
rs7132908	<i>FAIM2</i>	Extremely overweight young adults (GOYA Study)	Paternoster et al., PLOS One 2011	A	G	No proxy SNP						
rs2116830	<i>KCNMA1</i>	extreme obesity	Jiao et al. BMC Medical Genomics 2011	G	T	rs2116830	G	T	1.10 (1.00 - 1.22)	0.053047	0.8094765	0.793549
rs9299	<i>HOXB5</i>	childhood extreme obesity	Bradfield et al. Nat Genet 2012	T	C	No proxy SNP						
rs9568856	<i>OLFM4</i>	childhood extreme obesity	Bradfield et al. Nat Genet 2012	A	G	rs9568856	A	G	1.15 (1.01 - 1.29)	0.0281548	0.1361518	0.1192221
VARIANT p.R67C (rs61866610) <sup>†</sup>	<i>GPR120</i>	adult obesity	Ichimura et al. Nature 2012	T	C	rs61866610	T	C	0.90 (0.71 - 1.13)	0.36223	0.959058	0.96226
VARIANT p.R270H (rs116454156) <sup>†</sup>	<i>GPR120</i>	adult obesity	Ichimura et al. Nature 2012	A	G	Failed imputation QC						

**Supplementary Table 3. Results in GIANT for the SCOOP SNPs reaching genome-wide significance.** <sup>a</sup>Positions according to Build 36.

<sup>b</sup>rs2168711 used as a proxy in the replication stage.

**Supplementary Table 4. Results for GIANT SNPs in the SCOOP discovery analysis. Results not available for rs13107325, rs2287019, rs3810291, rs4771122 and rs4836133.**

SNP	Nearest gene	CHR	POS	Effect allele	Other allele	GIANT Discovery + Replication					SCOOP discovery (1509 cases, 5380 controls)			
						EAF	Effect	StdErr	N	P-value	OR (95% CI)	P-value	EAF cases	EAF controls
rs1558902	FTO	16	52,361,075	A	T	0.42	0.39	0.02	192,344	4.80E-120	1.48 (1.37 - 1.61)	2.02E-21	0.5039894	0.406029
rs2867125	TMEM18	2	612,827	C	T	0.83	0.31	0.03	197,806	2.77E-49	1.39 (1.25 - 1.55)	2.24E-09	0.8750828	0.8291822
rs571312	MC4R	18	55,990,749	A	C	0.24	0.23	0.03	203,600	6.43E-42	1.32 (1.20 - 1.45)	4.85E-09	0.2866136	0.2342761
rs543874	SEC16B	1	176,156,103	G	A	0.19	0.22	0.03	179,414	3.56E-23	1.22 (1.11 - 1.35)	0.0000428	0.248507	0.2132763
rs10767664	BDNF	11	27,682,562	A	T	0.78	0.19	0.03	204,158	4.69E-26	1.19 (1.08 - 1.31)	0.0004763	0.8094765	0.7799404
rs13107325	SLC39A8	4	103,407,732	T	C	0.07	0.19	0.04	245,378	1.50E-13				
rs10938397	GNPDA2	4	44,877,284	G	A	0.43	0.18	0.02	197,008	3.78E-31	1.21 (1.11 - 1.31)	5.51E-06	0.4817154	0.4343849
rs12444979	GPRC5B	16	19,841,101	C	T	0.87	0.17	0.03	239,715	2.91E-21	1.10 (0.98 - 1.24)	0.108095	0.8692615	0.8579821
rs11847697	PRKD1	14	29,584,863	T	C	0.04	0.17	0.05	241,667	5.76E-11	1.30 (1.06 - 1.58)	0.0104594	0.0521248	0.0415193
rs7359397	SH2B1	16	28,793,160	T	C	0.4	0.15	0.02	204,309	1.88E-20	1.07 (0.98 - 1.16)	0.132954	0.4113712	0.3969409
rs2287019	QPCTL	19	50,894,012	C	T	0.8	0.15	0.03	194,564	1.88E-16				
rs713586	RBJ	2	25,011,512	C	T	0.47	0.14	0.02	230,748	6.17E-22	1.07 (0.98 - 1.16)	0.111774	0.5102922	0.4936697
rs9816226	ETV5	3	187,317,193	T	A	0.82	0.14	0.03	196,221	1.69E-18	1.16 (1.05 - 1.3)	0.0051523	0.8451328	0.8222708
rs2815752	NEGR1	1	72,585,028	A	G	0.61	0.13	0.02	198,380	1.61E-22	1.25 (1.15 - 1.36)	7.64E-08	0.657389	0.6029931
rs987237	TFAP2B	6	50,911,009	G	A	0.18	0.13	0.03	195,776	2.90E-20	1.14 (1.03 - 1.27)	0.0139921	0.2001325	0.1803903
rs2241423	MAP2K5	15	65,873,892	G	A	0.78	0.13	0.02	227,950	1.19E-18	1.13 (1.03 - 1.25)	0.0137379	0.7968854	0.7758877
rs10150332	NRXN3	14	79,006,717	C	T	0.21	0.13	0.03	183,022	2.75E-11	1.04 (0.94 - 1.15)	0.412038	0.2253662	0.2183309
rs7138803	FAIM2	12	48,533,735	A	G	0.38	0.12	0.02	200,064	1.82E-17	1.23 (1.13 - 1.34)	1.02E-06	0.416501	0.3671628
rs10968576	LRRN6C	9	28,404,339	G	A	0.31	0.11	0.02	216,916	2.65E-13	1.04 (0.95 - 1.13)	0.417641	0.3272425	0.31984
rs2112347	FLJ35779	5	75,050,998	T	G	0.63	0.1	0.02	231,729	2.17E-13	1.06 (0.97 - 1.15)	0.203787	0.6513113	0.6400378
rs887912	FANCL	2	59,156,381	T	C	0.29	0.1	0.02	242,807	1.79E-12	1.00 (0.91 - 1.09)	0.924522	0.2983278	0.300448
rs13078807	CADM2	3	85,966,840	G	A	0.2	0.1	0.02	237,404	3.94E-11	1.04 (0.94 - 1.15)	0.419845	0.2009409	0.19288
rs3810291	TMEM160	19	52,260,843	A	G	0.67	0.09	0.02	233,512	1.64E-12				
rs2890652	LRP1B	2	142,676,401	C	T	0.18	0.09	0.03	209,068	1.35E-10	1.23 (1.10 - 1.38)	0.0002536	0.1813003	0.1534431
rs4771122	MTIF3	13	26,918,180	G	A	0.24	0.09	0.03	198,577	9.48E-10				
rs1514175	TNNI3K	1	74,764,232	A	G	0.43	0.07	0.02	227,900	8.16E-14	1.19 (1.09 - 1.28)	0.0000359	0.4738237	0.4312686
rs4836133	ZNF608	5	124,360,002	A	C	0.48	0.07	0.02	241,999	1.97E-09				
rs3817334	MTCH2	11	47,607,569	T	C	0.41	0.06	0.02	191,943	1.59E-12	1.02 (0.94 - 1.10)	0.711429	0.4102054	0.4059535
rs1555543	PTBP2	1	96,717,385	C	A	0.59	0.06	0.02	243,013	3.68E-10	1.04 (0.95 - 1.12)	0.397028	0.594496	0.5865886
rs4929949	RPL27A	11	8,561,169	C	T	0.52	0.06	0.02	249,791	2.80E-09	1.04 (0.96 - 1.13)	0.352953	0.5485872	0.54071
rs29941	KCTD15	19	39,001,372	G	A	0.67	0.06	0.02	192,872	3.01E-09	1.07 (0.98 - 1.16)	0.145136	0.6929474	0.6778274
rs206936	NUDT3	6	34,410,847	G	A	0.21	0.06	0.02	249,777	3.02E-08	1.02 (0.92 - 1.12)	0.761386	0.1961564	0.1937523

**Supplementary Table 5. Global CNV burden analysis of >100kb rare CNVs: event type and size.  $P_{MAD}$ ,  $P_{NCPS}$ : P values derived from permutation conditioned on MAD of samples log2ratio or number of calls per sample.**

Type	Size (kb)	Case rate	Case/control ratio	$P_{MAD}$	$P_{NCPS}$
Losses and gains	100-200	0.9731	1.1984	0.0000	0.0000
	200-500	0.5720	1.0504	0.1104	0.0329
	>500	0.1988	1.1658	0.0205	0.0057
Losses	100-200	0.3733	1.1122	0.0165	0.0082
	200-500	0.1762	1.0074	0.4438	0.3395
	>500	0.0477	1.4357	0.0117	0.0076
Gains	100-200	0.5998	1.2590	0.0000	0.0000
	200-500	0.3958	1.0707	0.0953	0.0339
	>500	0.1510	1.1004	0.1446	0.0653

**Supplementary Table 6. Pathway enrichment analysis of rare genic obesity CNVs. All enrichment pathways reaching statistical significance are shown (p-value <0.05), according to the respective functional enrichment algorithm (Ingenuity Pathways Analysis (IPA), Panther, GOTERM). The subcategories of the most significantly associated category (Nervous system development and function) are listed separately.**

Pathways geneset	Functional enrichment algorithm	Number of genes	P-Value
<b>Nervous System Development and Function</b>			
GPCR_Gα12/13 Signaling	IPA	15	1.71E-04
Sphingosine-1-phosphate Signaling	IPA	12	2.21E-03
CREB Signaling in Neurons	IPA	16	2.71E-03
Neuropathic Pain Signaling In Dorsal Horn Neurons	IPA	11	3.00E-03
Glutamate Receptor Signaling	IPA	8	3.70E-03
Synapse component	GOTERM	15	1.80E-02
Histamine H1 receptor mediated signaling pathway	PANTHER_PATHWAY	4	2.70E-02
Synaptic transmission	PANTHER	11	3.70E-02
Neuronal activities	PANTHER	18	3.80E-02
Notch signaling pathway	PANTHER_PATHWAY	4	4.30E-02
Oxytocin receptor mediated signaling pathway	PANTHER_PATHWAY	4	4.40E-02
Heterotrimeric G-protein signaling pathway-Gq alpha and Gαo	PANTHER_PATHWAY	6	4.90E-02
Axon guidance mediated by Slit/Robo	PANTHER_PATHWAY	3	9.40E-02

**Nervous System Development and Function (p-value p=0.0000983)**

Functions Annotation subcategory	Functional enrichment algorithm	Number of genes	p-Value
projection of sensory neurons	IPA	4	2.67E-06
synaptic transmission of neurons	IPA	23	2.94E-05
analgesia	IPA	10	1.78E-04
assembly of synapse	IPA	7	1.95E-04
antinociception	IPA	6	4.97E-04
synaptic transmission	IPA	24	6.01E-04
branching of neurites	IPA	15	1.15E-03
chemorepulsion of neurons	IPA	3	1.21E-03
long term depression of Purkinje cells	IPA	3	1.21E-03
neuritogenesis	IPA	31	1.29E-03
guidance of corticofugal axons	IPA	2	1.64E-03
guidance of corticothalamic axons	IPA	2	1.64E-03
projection of retinal ganglion cells	IPA	2	1.64E-03
dendritic growth/branching	IPA	12	1.79E-03
long-term potentiation of hippocampal cells	IPA	5	3.49E-03
long-term potentiation of pyramidal neurons	IPA	4	4.17E-03
chemorepulsion of commissural neurons	IPA	2	4.78E-03
long-term potentiation of synapse	IPA	5	5.69E-03
development of neural crest	IPA	4	6.37E-03
reflex	IPA	5	6.61E-03
guidance of axons	IPA	12	7.83E-03
long-term potentiation of neurons	IPA	7	7.91E-03
pathfinding of nervous tissue	IPA	3	8.56E-03
guidance of thalamocortical axons	IPA	2	9.31E-03
inhibition of pyramidal neurons	IPA	2	9.31E-03
memory	IPA	13	9.92E-03
axonogenesis of organism	IPA	3	1.40E-02
long-term potentiation of CA1 neuron	IPA	3	1.40E-02
development of glossopharyngeal nerve	IPA	2	1.51E-02
flexor reflex	IPA	2	1.51E-02
long-term potentiation of collateral synapses	IPA	2	1.51E-02
long-term potentiation	IPA	12	1.73E-02
synaptogenesis	IPA	11	1.94E-02
development of brain	IPA	25	2.16E-02
loss of neurons	IPA	8	2.46E-02
growth of axons	IPA	9	2.66E-02
differentiation of oligodendrocytes	IPA	7	2.81E-02
density of dendritic spines	IPA	4	2.84E-02
quantity of dopaminergic neurons	IPA	3	2.95E-02
axonogenesis	IPA	11	2.97E-02
contact repulsion of axons	IPA	2	3.01E-02
development of sensory projections	IPA	2	3.01E-02
extension of dendrites	IPA	2	3.01E-02
loss of striatal neurons	IPA	2	3.01E-02

**Supplementary Table 7.** Pathway enrichment analysis of rare genic obesity CNVs. Geneset enrichment p-values for each of the enriched pathway categories are shown (p-value <0.05).

Pathway geneset	Database	Number of genes	p (intercept)	p (number CNV)	p (CNV size)	p (Raychaudhuri et al., PLoS Gen (2010))
Cell cycle (mitotic)	Reactome	306	3.30875E-08	5.24661E-17	0.006666444	1.66093E-07
G-alpha-i signalling events	Reactome	177	6.31756E-08	1.17509E-16	0.007810423	3.11599E-06
Mitotic m m g1 phases	Reactome	157	7.41219E-08	1.3558E-16	0.010805037	5.18423E-06
Centrosome maturation	Reactome	72	8.76589E-08	2.23696E-16	0.008524619	5.48418E-06
G2-M transition	Reactome	84	9.24842E-08	2.20084E-16	0.009229	1.51296E-05
Downstream events in GPCR signaling	Reactome	448	4.13953E-08	4.87285E-17	0.008332325	3.60315E-05
PtdIns pathway	Biocarta	23	1.93E-07	2.78E-16	0.020667568	7.09E-05
Mitotic prometaphase	Reactome	92	1.09E-07	2.45E-16	0.011682378	8.48E-05
NOTCH signaling pathway	KEGG	47	1.16E-07	1.23E-16	0.019369464	0.000100251
Loss of nlp from mitotic centrosomes	Reactome	62	1.59E-07	3.39E-16	0.01396758	0.00012509
<b>GPCR ligand binding</b>	<b>Reactome</b>	<b>392</b>	<b>7.84E-08</b>	<b>1.30E-16</b>	<b>0.009636133</b>	<b>0.000188367</b>
Insulin receptor pathway in cardiac myocytes	Reactome	49	9.63E-08	1.69E-16	0.010682659	0.000205434
Peptide ligand binding receptors	Reactome	173	1.12E-07	2.11E-16	0.011158427	0.000206803
Akapcentrosome pathway	Biocarta	15	2.09E-07	4.02E-16	0.017845113	0.000234468
Integrin pathway	Biocarta	38	9.68E-08	3.12E-16	0.008576578	0.000243165
Insulin signaling pathway	KEGG	137	7.11E-08	1.08E-16	0.011370679	0.00026303
Neuroactive ligand receptor interaction	KEGG	272	9.93E-08	1.34E-16	0.011638387	0.000273527
Glucose and other sugar slc transporters	Reactome	82	2.67E-07	5.81E-16	0.01813577	0.000415675
Chronic myeloid leukemia	KEGG	73	7.60E-08	1.39E-16	0.010663623	0.000446214
trkA signalling from the plasma membrane	Reactome	103	1.13E-07	1.57E-16	0.015494824	0.000500949
Regulation of actin cytoskeleton	KEGG	216	7.50E-08	1.10E-16	0.011448296	0.000569708
Peroxisome	KEGG	78	1.43E-07	2.93E-16	0.013454998	0.000760129
Gleevac pathway	Biocarta	23	1.09E-07	2.22E-16	0.012401503	0.000772304
Axon guidance	KEGG	129	1.59E-07	1.56E-16	0.021652624	0.000914917
Muscle contraction	Reactome	51	1.33E-07	3.02E-16	0.012811725	0.001123512
G1 pathway	Biocarta	28	1.65E-07	2.71E-16	0.01868521	0.001313421
Ionotropic activity of kainate receptors	Reactome	12	1.87E-07	3.09E-16	0.018967072	0.001388892
IL2R-beta pathway	Biocarta	38	1.04E-07	1.73E-16	0.013787	0.001427232
Class A1 rhodopsin-like receptors	Reactome	292	1.01E-07	2.10E-16	0.010076066	0.00146531
Breast cancer	Biocarta	334	1.38E-07	1.90E-16	0.0156521	0.001508042
Metal ion slc transporters	Reactome	23	2.29E-07	3.86E-16	0.021176259	0.00152129
Smooth muscle contraction	Reactome	24	1.35E-07	2.85E-16	0.013688021	0.001600053
Class B2 secretin family receptors	Reactome	85	1.71E-07	1.90E-16	0.024097338	0.001767936
ERK pathway	Biocarta	28	1.74E-07	2.79E-16	0.018237955	0.001819427
MAPK pathway	Biocarta	87	1.42E-07	1.85E-16	0.018052711	0.001903258
Calcitonin like ligand receptors	Reactome	10	2.33E-07	2.50E-16	0.028755115	0.001927829
G-protein activation	Reactome	28	1.66E-07	2.48E-16	0.019295505	0.002198655
Transmembrane transport of small molecules	Reactome	218	2.79E-07	3.88E-16	0.022167625	0.002481027
RacCYCD pathway	Biocarta	26	2.14E-07	4.16E-16	0.018238989	0.002703144
Prostanoid hormones	Reactome	11	1.61E-07	4.27E-16	0.013047454	0.002757851
Glycolysis	Reactome	22	2.44E-07	4.65E-16	0.019578786	0.002962656
Glycolysis Gluconeogenesis	KEGG	62	2.24E-07	3.13E-16	0.022185423	0.003014437
SLC mediated transmembrane transport	Reactome	169	3.21E-07	4.53E-16	0.023902273	0.003059199
Zinc transportation	Reactome	17	1.99E-07	3.58E-16	0.019168402	0.00321331
Glutathione metabolism	KEGG	50	4.79E-07	8.40E-16	0.026040162	0.003279803
Vascular smooth muscle contraction	KEGG	115	1.45E-07	2.46E-16	0.0150341	0.003474145
MAPK signaling pathway	KEGG	267	1.11E-07	1.49E-16	0.015429059	0.003487917
CD40 pathway map	Reactome	33	2.36E-07	4.38E-16	0.019409452	0.004265294
Formation of fibrin clot clotting cascade	Reactome	32	1.43E-07	2.69E-16	0.015542979	0.00454064
Vitamin B5 (pantothenate) metabolism	Reactome	11	2.19E-07	3.47E-16	0.02128256	0.004593501
HER2 pathway	Biocarta	22	2.66E-07	3.72E-16	0.023167878	0.004706068
Downstream signal transduction	Reactome	35	1.19E-07	2.01E-16	0.014798131	0.004756173
Fructose and Mannose metabolism	KEGG	34	2.82E-07	5.06E-16	0.021260545	0.005106532
MPR pathway	Biocarta	34	2.11E-07	4.00E-16	0.018265761	0.005524797
Acute myeloid leukemia	KEGG	60	1.38E-07	2.10E-16	0.017215513	0.005563321
ActinY pathway	Biocarta	20	1.69E-07	2.32E-16	0.021526719	0.005734309
G alpha s signalling events	Reactome	126	1.43E-07	1.92E-16	0.018291446	0.006852951
Recruitment of numa to mitotic centrosomes	Reactome	11	1.98E-07	4.24E-16	0.016019914	0.006865837
AKT pathway	Biocarta	22	2.93E-07	5.28E-16	0.022279641	0.006931782
G alpha s pathway	Reactome	12	2.66E-07	4.67E-16	0.022006929	0.006985946
Gene expression	Reactome	425	1.27E-07	2.09E-16	0.014387299	0.007044607
Zinc influx into cells by the SLC39 genes family	Reactome	10	2.24E-07	3.29E-16	0.023060811	0.007372643
p38 mapk pathway	Reactome	35	2.01E-07	3.23E-16	0.020000003	0.007380184
ABC transporters	KEGG	44	1.70E-07	3.50E-16	0.015431234	0.00815356
Signaling by Robo receptor	Reactome	32	2.37E-07	3.15E-16	0.023766553	0.008757844
TGF-beta signaling pathway	KEGG	86	1.98E-07	3.38E-16	0.017776025	0.008771479
Axon guidance	Reactome	161	1.53E-07	2.22E-16	0.016949584	0.009494267
BAD pathway	Biocarta	26	2.75E-07	5.76E-16	0.019666344	0.010025752
p53 hypoxia pathway	Biocarta	23	2.01E-07	3.16E-16	0.021275891	0.010234892
Apoptosis	Reactome	129	2.23E-07	2.84E-16	0.023938507	0.01029615
TNFR1 pathway	Biocarta	29	1.98E-07	2.61E-16	0.023593695	0.010342409
HIF pathway	Biocarta	15	2.10E-07	2.98E-16	0.023146802	0.010412612
Apoptotic cleavage of cell adhesion proteins	Reactome	11	2.44E-07	4.01E-16	0.021980747	0.010892905
ARF pathway	Biocarta	17	2.67E-07	3.55E-16	0.026711577	0.011231898
Genes involved in apoptotic cleavage of cellular proteins	Reactome	37	2.37E-07	3.73E-16	0.021954081	0.011271364
Glycosaminoglycan biosynthesis heparan sulfate	KEGG	26	1.87E-07	3.99E-16	0.016495852	0.011347531
Activation of Rac	Reactome	14	3.38E-07	4.91E-16	0.0271174	0.011495833
HIV infection	Reactome	183	1.67E-07	1.98E-16	0.021381992	0.011537561
Signaling by PDGF	Reactome	64	1.56E-07	2.80E-16	0.015895745	0.012030348
G alpha-z signalling events	Reactome	14	2.08E-07	3.35E-16	0.020447299	0.012411238

CDC20 phospho APC mediated degradation of cyclin A	Reactome	63	2.49E-07	3.58E-16	0.024051914	0.012416861
PI3K AKT signalling	Reactome	37	1.94E-07	2.62E-16	0.022009292	0.012699778
TGFB pathway	Biocarta	19	2.38E-07	4.30E-16	0.01957655	0.012923816
FAS signaling pathway	Reactome	59	2.40E-07	3.40E-16	0.023652607	0.013398465
Cell cycle checkpoints	Reactome	110	2.23E-07	3.55E-16	0.020702284	0.01349103
Elongation and processing of capped transcripts	Reactome	134	1.61E-07	2.14E-16	0.020090229	0.013592384
Processing of capped intron containing pre Mrna	Reactome	138	1.94E-07	3.19E-16	0.018631053	0.013625094
Metabolism of vitamins and cofactors	Reactome	42	2.58E-07	4.25E-16	0.021735447	0.013769948
Prostate cancer	KEGG	89	1.85E-07	2.80E-16	0.019011715	0.013810848
Glucose metabolism	Reactome	56	1.89E-07	4.02E-16	0.016074089	0.01462883
Caspase pathway	Biocarta	23	2.59E-07	3.87E-16	0.024358754	0.014888815
Regulation of beta cell development	Reactome	114	2.36E-07	4.63E-16	0.018551204	0.015093369
Activation of kainate receptors upon glutamate binding	Reactome	32	1.99E-07	3.24E-16	0.019717504	0.01532806
Neurotrophin signaling pathway	KEGG	126	1.52E-07	2.59E-16	0.016447165	0.016502778
Formation and maturation of mrna transcript	Reactome	152	1.71E-07	2.27E-16	0.020593875	0.017007939
ALK pathway	Biocarta	37	3.00E-07	3.51E-16	0.028646937	0.017243247
Signalling by NGF	Reactome	215	1.52E-07	2.05E-16	0.017950369	0.017266432
G2 pathway	Biocarta	24	2.55E-07	3.58E-16	0.025201438	0.017378819
mRNA splicing	Reactome	107	1.74E-07	2.64E-16	0.019278984	0.01744546
Inactivation of APC via direct inhibition of the apcomplex	Reactome	18	2.93E-07	5.10E-16	0.023391959	0.017585511
mRNA 3'-end processing	Reactome	34	2.41E-07	4.24E-16	0.020782471	0.017807137
IGF1R pathway	Biocarta	23	3.05E-07	6.93E-16	0.019917707	0.018131661
ERK1 ERK2 MAPK pathway	Reactome	29	2.42E-07	4.65E-16	0.019152896	0.018330854
Cell cycle	KEGG	128	1.78E-07	2.90E-16	0.018742156	0.01956934
Fatty acid metabolism	KEGG	42	2.49E-07	3.96E-16	0.022670572	0.020138296
CTCF pathway	Biocarta	23	2.29E-07	2.65E-16	0.026252985	0.020225877
TFF pathway	Biocarta	21	3.24E-07	7.31E-16	0.020346377	0.020319621
Olfactory transduction	KEGG	389	2.05E-07	3.85E-16	0.016794753	0.020453977
SEMA4D induced cell migration and growth cone collapse	Reactome	24	1.89E-07	3.30E-16	0.018264922	0.020580169
Endocytosis	KEGG	183	1.62E-07	1.96E-16	0.020343968	0.020859613
ERBB signaling pathway	KEGG	87	1.58E-07	2.49E-16	0.016634667	0.021401669
MET pathway	Biocarta	37	1.54E-07	2.69E-16	0.01629783	0.021447568
AKT phosphorylates targets in the cytosol	Reactome	14	2.67E-07	4.25E-16	0.023607473	0.021450774
Bladder cancer	KEGG	42	2.60E-07	4.87E-16	0.020553008	0.021490944
Prion diseases	KEGG	35	2.75E-07	4.48E-16	0.022212637	0.02253312
Tumor necrosis factor pathway	Reactome	28	2.57E-07	3.72E-16	0.02483723	0.024132032
Generic transcription pathway	Reactome	35	1.75E-07	3.35E-16	0.016573794	0.024141832
Oxidative phosphorylation	KEGG	135	2.11E-07	3.37E-16	0.019568995	0.025053574
Regulation of apc activators between g1 s and early anaphase	Reactome	71	2.72E-07	3.84E-16	0.025288646	0.02512877
NTHI pathway	Biocarta	24	2.31E-07	3.31E-16	0.023011625	0.025611106
Host interactions of HIV factors	Reactome	120	2.17E-07	3.12E-16	0.021731567	0.025674942
Olfactory signaling pathway	Reactome	371	2.14E-07	3.99E-16	0.01758899	0.026798743
Glycosaminoglycan biosynthesis chondroitin sulfate	KEGG	22	2.15E-07	4.18E-16	0.01883905	0.027725526
Glycosphingolipid biosynthesis globo series	KEGG	14	3.62E-07	6.51E-16	0.024401831	0.029911338
CD40 pathway	Biocarta	15	2.12E-07	3.04E-16	0.022909624	0.029990802
Calpain pathway	Biocarta	18	2.72E-07	4.55E-16	0.022978289	0.031275743
Signaling by NOTCH	Reactome	16	2.70E-07	4.06E-16	0.024111809	0.032549497
M G1 transition	Reactome	61	2.52E-07	3.39E-16	0.02584788	0.033400688
Ethanol oxidation	Reactome	10	2.91E-07	4.49E-16	0.025272596	0.033546691
Abortive elongation of HIV1 transcript in the absence of tat	Reactome	23	2.16E-07	3.30E-16	0.021811885	0.033579242
Amino-sugar and nucleotide-sugar metabolism	KEGG	44	2.94E-07	4.91E-16	0.023225317	0.033772758
Transport of mature mRNA derived from an intron-containing transcript	Reactome	51	3.06E-07	5.94E-16	0.021379557	0.033890104
HSL mediated triacylglycerol hydrolysis	Reactome	12	2.23E-07	3.38E-16	0.022722864	0.034704321
FAS pathway	Biocarta	30	2.78E-07	3.74E-16	0.027194239	0.034803436
HIV life cycle	Reactome	103	2.06E-07	3.15E-16	0.020416011	0.034889781
apoptotic execution phase	Reactome	48	2.36E-07	3.39E-16	0.023210072	0.0351862
pathways in cancer	KEGG	328	1.36E-07	1.69E-16	0.018446236	0.035349708
maturity onset diabetes of the young	KEGG	25	3.44E-07	6.82E-16	0.023309942	0.035407339
proximal tubule bicarbonate reclamation	KEGG	23	2.63E-07	3.93E-16	0.02466266	0.035969243
autodegradation of cdh1 by cdh1 apc	Reactome	57	2.58E-07	3.89E-16	0.023848608	0.036117697
IGF1 pathway	Biocarta	21	3.14E-07	6.86E-16	0.020744264	0.036513205
D4GDI pathway	Biocarta	13	3.18E-07	4.53E-16	0.02763268	0.037003974
Glucose regulation of insulin secretion	Reactome	161	1.85E-07	2.76E-16	0.019320215	0.037237895
RNA polymerase II transcription	Reactome	92	2.13E-07	2.91E-16	0.02264099	0.037779534
MAL pathway	Biocarta	19	2.76E-07	5.53E-16	0.020602926	0.037809015
Basigin interactions	Reactome	25	3.35E-07	6.38E-16	0.023028274	0.038314458
TOB1 pathway	Biocarta	21	2.79E-07	3.73E-16	0.026462332	0.038507006
Gluconeogenesis	Reactome	31	2.00E-07	4.15E-16	0.01700908	0.038679294
Biopeptides pathway	Biocarta	43	2.12E-07	3.06E-16	0.021993274	0.038837347
Myocyte ad pathway	Reactome	23	3.05E-07	5.15E-16	0.024120734	0.03893729
PPARA pathway	Biocarta	58	2.12E-07	3.37E-16	0.020116517	0.039195351
Platelet degranulation	Reactome	86	2.53E-07	5.33E-16	0.018481784	0.040344395
Diabetes pathways	Reactome	383	1.75E-07	2.91E-16	0.017110136	0.040480888
IL3 pathway	Biocarta	15	2.73E-07	4.37E-16	0.023137733	0.040523677
Parkinsons disease	KEGG	133	2.10E-07	3.31E-16	0.019433732	0.041325245
Lysine degradation	KEGG	44	2.20E-07	3.47E-16	0.021091148	0.042435772
Oocyte meiosis	KEGG	114	2.37E-07	3.83E-16	0.020988658	0.042507468
WNT beta-catenin pathway	Reactome	31	2.66E-07	5.02E-16	0.020891316	0.0428662
Pyrimidine catabolism	Reactome	10	2.62E-07	4.91E-16	0.021318198	0.043889082
Late phase of hiv life cycle	Reactome	90	2.10E-07	3.30E-16	0.020340479	0.044289797
PS1 pathway	Biocarta	14	2.79E-07	4.00E-16	0.025151775	0.045056005
Drug metabolism cytochrome p450	KEGG	72	4.16E-07	6.35E-16	0.026905067	0.048232597
Lysosome	KEGG	121	2.31E-07	3.24E-16	0.02187226	0.048786262
Type II diabetes mellitus	KEGG	47	2.24E-07	4.02E-16	0.019119615	0.049333223

**Supplementary Table 8.** Oligonucleotides used for the EMSA experiment

Primer	Forward Sequence (5'-3')	Reverse Sequence (5'-3')
NKX6.1_8del_WT	GATCTGTCAGTTTAATTGGATTATAAGGTAA	TTACCTTATAAAATCCAATTAAAATGACAGATC
NKX6.1_8del_MUT	GATCTGTCAGTGGCCGGTTCGTTATAAGGTAA	TTACCTTATAACGAACCGGCCACTGACAGATC

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